



PATENT

RESPONSE UNDER 37 C.F.R. 1.116 - EXPEDITED
PROCEDURE - EXAMINING GROUP 1632

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.: 09/689,430
Applicants: Walsh *et al.*
Filed: October 12, 2000
Art Unit: 1632
Examiner: Quian J. Li
Title: ADENO-ASSOCIATED VIRUS VECTORS ENCODING
FACTOR VIII AND METHODS OF USING THE SAME

Confirmation No.: 7095

Docket No.: 35052/204373(5052-53)

Customer No.: 00826

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INTERVIEW SUMMARY

Sir:

A telephonic interview in the above-referenced matter occurred on September 2, 2003 between Examiner Li, Examiner Wehbe', Applicants' representatives Murray Spruill and Kathryn Coulter, Kim Wietes Clary (from Targeted Genetics, the licensee for the present application), and Catherine Polizzi (licensee's representative). Applicants provide a summary of the interview below.

The discussion focused on claim 1, although some issues discussed are relevant to other claims. The prior art references discussed were U.S. Patent No. 6,221,646 to Dwarki *et al.*; Zhang *et al.* (1998) *Proc. Natl. Acad. Sci. USA* 95:10158-63; and Flotte *et al.* (1993) *J. Biol. Chem.* 268:3781-3790.

With regards to Dwarki *et al.*, Applicants' representatives pointed out that while this patent teaches AAV virions with a heterologous gene positioned between two AAV ITRs and suggests that Factor VIII may be expressed using such a vector, and further teaches and

exemplifies the use of promoters and other control regions to control expression of the heterologous gene in an AAV vector, it does not teach the use of the ITR and an enhancer to drive transcription of a heterologous gene, where the ITR is the only promoter. Rather, the reference teaches that ITRs are included in the vector because they are needed for replication and packaging. Applicants pointed to line 66 of column 4 through line 2 of column 5 of this patent for support for this statement. Furthermore, the patent does not teach the expression of B-domain deleted factor VIII.

With regards to Zhang *et al.*, Applicants' representatives discussed the fact that this reference teaches the use of an AAV ITR as the only promoter to express CFTR, but also teaches that very low levels of expression are obtained when the ITR is used. The reference is directed to determining the regions of the CFTR gene that may be deleted to make room for a more efficient promoter. Figure 3 of this reference, which shows a comparison of the CFTR expression levels obtained using an AAV ITR and the AAV p5 promoter to drive expression and illustrates the low levels of expression obtained with the AAV ITR, was discussed.

Examiner Li asked about the teachings of the Flotte *et al.* reference, which is cited by Zhang *et al.* and is also cited as reference 84 on Applicants' Information Disclosure Statement filed February 21, 2003. Kim Clary explained that this reference teaches that the AAV ITR has transcriptional activity, but does not teach the use of an ITR combined with an enhancer to drive expression of a transgene.

Examiner Li stated that in her view of the case, there were two issues to be considered: 1) whether there was motivation to combine an ITR and enhancer; and 2) whether claim 1 should be amended to recite a particular level of expression. Applicants pointed out that it was not necessary for claim 1 to recite a particular level of expression to overcome the rejection because the art provided no suggestion or motivation to make the invention of claim 1.

Examiner Wehbe' suggested that Applicants, in replying to the final office action, should focus their arguments on the teachings of Dwarki *et al.* with respect the function of the ITR in the described AAV vector, and on the fact that Zhang *et al.* teach away from using an ITR and enhancer to drive transcription of a transgene. Examiner Li will then consider our response.

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It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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<p>Customer No. 00826 ALSTON & BIRD LLP Bank of America Plaza 101 South Tryon Street, Suite 4000 Charlotte, NC 28280-4000 Tel Raleigh Office (919) 862-2200 Fax Raleigh Office (919) 862-2260</p>	<p><u>CERTIFICATE OF EXPRESS MAILING</u> "Express Mail" mailing label number EV184328759US Date of Deposit December 4, 2003 I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 <i>Nora C. Martinez</i> _____ Nora C. Martinez</p>
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